REMARKS

Claims 1-21 are pending and stand rejected. Applicant has amended the specification such that each letter of a trademark is capitalized in response to the Examiner's objections regarding the use of trademarks. Applicant has amended independent claims 1 and 20 to recite that the first and second labels are different. Support for this amendment can be found, for example, at page 11, lines 5-6. Applicant respectfully requests entry of the above amendments, which raise no issues that would require further consideration and/or search, and which place the application in better condition for allowance. Applicant respectfully requests reconsideration and allowance of claims 1-21 in view of the above amendments and following remarks.

Rejections under 35 U.S.C. § 103

The Examiner maintained the rejection of claims 1-21 under 35 U.S.C. § 103(a) as being unpatentable over Kortright, et al. (U.S. Patent No. 4,870,003) in view of Jackson, et al. (U.S. Patent No. 5,776,709). The Examiner asserted that "Applicant is arguing limitations not found in the claims which do not require that the 'first' and 'second' labels are different." The Examiner also contended that "it would have been obvious to one of skill in the art to use the fluorochrome labeling disclosed by Jackson et al. in the methods disclosed by Kortright et al. in order to reap the benefits of direct measurement (both qualitative and quantitative) of each label (and hence each binding pair member) as well as the reduction in sample preparation and data acquisition. One would have a reasonable expectation of success since Kortright et al. suggest the use of other labeling systems, specifically 'fluorescers' (see column 7 lines 29-32)." Applicant respectfully traverses.

The present invention provides a rapid and sensitive method that can be used to enhance the ability to detect infection or other pathologies at an early stage, leading to earlier treatments. Independent claim 1 recites a method for simultaneously measuring both members A and B of a binding pair in a biological sample, while independent claim 20 recites a kit for simultaneously measuring both members A and B of a binding pair. The method includes:

a) providing a solid phase reagent, the solid phase reagent comprising a particle coated with capture antibodies having specific binding affinities for member A of the binding pair;

b) contacting the biological sample with the solid phase reagent under conditions in which member A, if present, becomes bound to the particle, to form a first reacted particle;

c) contacting the first reacted particle with first antibodies having specific binding affinities for member A, wherein the first antibodies are labeled with a first label, and with second antibodies having specific binding affinities for member B of the binding pair, wherein the second antibodies are labeled with a second label, to form a second reacted particle, and

d) measuring the first and second labels on the second reacted particle using flow cytometry.

In contrast to the Examiner's assertions, the first and second labels recited in independent claims 1 and 20 are different. As indicated in the specification at page 11, lines 5-6, "[e]ach labeled antibody can be distinctly visualized by labeling with a fluorophore that emits light of a color that contrasts with other fluorophores." Thus, Applicant is arguing limitations that are found in the claim. Nevertheless, solely to expedite prosecution of the application, Applicant has amended claims 1 and 21 to recite that the first and second labels are different. Applicant notes that this amendment does not change the scope of original claim 1.

The combination of the '003 patent and '709 patent does not teach or suggest the presently claimed methods or kits. The '003 patent discloses a system for detecting HIV antigen and anti-HIV antibody that includes capturing viral antigen with an immobilized anti-HIV antibody and detecting with a biotin-labeled, human, anti-HIV antibody. A known concentration of viral antigen is added to the patient's sample prior to the assay. The '709 patent discloses a flow cytometry method for analyzing populations of leukocytes that uses two or more fluorescent labels. Leukocytes are identified by combinations of cell surface markers.

The '003 patent does not teach or suggest that two antibodies, one having specificity for member A and one having specificity for member B, that are differentially labeled can be used to simultaneously detect both members of a binding pair. In contrast, the presence of one of the members of the binding pair is determined indirectly in the '003 patent by spiking the samples with viral antigen and noting if the spiked antigen increases or decreases optical density. See, column 3, lines 42 - 61 of the '003 patent, which explain the rational for the '003 assay. More specifically, the assay of the '003 patent spikes a known concentration of virus antigen into the serum or plasma sample. If antibody is present in the sample, the antibody will bind to the

spiked viral antigen and will interfere with the detection of the spiked viral antigen. If less than the known amount of antigen is detected, the sample is construed to be "antibody positive". If the antigen spike has an additive effect with the sample, the sample is construed to be "antigen positive". If the concentration of the spiked sample is measured to be the same as the known amount of the spike, then the sample is construed to be "negative for both antibody and antigen". Thus, the underlying premise of the '003 patent is that host antibody present in the sample will interfere with the results of the assay. Consequently, any antibody present in the sample will interfere with the actual quantitation of the analyte in that assay system and the assay can do no more than determine if there is "free" antigen present or "free" antibody (free meaning unbound to antibody or antigen, or other interfering substance). Therefore, the assay of the '003 patent is unable to detect an immune complex of virus and antibody.

In contrast to the assay of the '003 patent, the present assay allows both members of a binding pair to be directly and simultaneously measured since, with respect to the present claims, the first antibody and member B (e.g., host antibody) do not functionally interfere with each other's binding to member A. Step C of amended claim 1 recites that a second reacted particle is formed by contacting the first reacted particle (capture antibody and member A) with a first labeled antibody and a second labeled antibody. To form the second reacted particle, the first antibody must be able to bind member A without functional interference from member B. This is exactly the opposite of the underlying premise of the assay disclosed in the '003 patent, which is based on interference by host antibody.

The '709 patent does not remedy the deficiencies of the '003 patent, as the '709 patent does not teach or suggest that both members of a binding pair can be measured simultaneously. In fact, the '709 patent does not even measure a binding pair. Subpopulations of leukocytes are measured with antibodies that bind to different cell surface markers. Using multiple fluorescent markers in the assay disclosed in the '003 patent still does not allow one to measure both members of a binding pair. Again, the assay disclosed in the '003 patent only indirectly determines if antibody is present and does not allow one to simultaneously measure both members of a binding pair. As the combination of the '003 and '709 patents does not teach the simultaneous measurement of both members of a binding pair, Applicant submits that the present

claims are non-obvious. The Examiner is respectfully requested to withdraw the rejection of claims 1-21 under 35 U.S.C. §103.

CONCLUSION

Applicant respectfully requests reconsideration and prompt allowance of the pending claims. The Examiner is invited to telephone the undersigned if it is felt that such would advance prosecution of the application.

No fees are required as the response is being filed before the three-month date. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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